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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,765	11/08/2001	Preben Christensen	60123.000002	4417

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EXAMINER

SAUCIER, SANDRA E

ART UNIT PAPER NUMBER

1651

DATE MAILED: 02/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/914,765

Applicant(s)

Christensen et al.

Examiner

Sandra Saucier

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-44 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirements.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6 6) ☐ Other: _____

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DETAILED ACTION

Claims 1-44 are pending and are considered on the merits.

Claim Rejections – 35 USC § 112

INDEFINITE

Claims 1-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is intended by the recitation of “in the same determination routine” in claim 1, especially since a second determination can be made with a “subsample”.

It is unclear what period of time is encompassed by the use of the phrase “substantially simultaneously” in claim 2. Does one second, minute, hour, day or week, etc. fall within or without the boundaries of the claim? The lack of a definition in the specification makes this limitation ambiguous.

Claim 12 uses the abbreviation, MPR71292. A search of the Chemical Abstracts Registry of Chemicals database shows no results for this “name”. Therefore, it cannot be determined for what compound applicants intend this abbreviation to stand. The claim is, therefore, not interpretable and has not been examined for art purposes.

Further, claim 12 uses “ethidium-homodimer-2, EHD2”. Please delete “EHD2” as either being repetitious or confusing or an attempt at expanding or further limiting the previous phrase.

Claim 13 is indefinite because it does not incorporate a concentration, but merely states that the concentration is that which is less than routinely used. This is not a concentration limitation which has definite metes and bounds.

Claim 14 has no antecedent basis for the recitation “staining all sperm cells”.

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Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action: A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent, (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1–6, 9, 13, 16–19, 31, 32, 33, 36, 39, 41, 43 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by GB 2 214 518 [J].

The claims are directed to a method of determining sperm concentration and % viability by selective staining in the same sample or subsample and in the same determinative routine.

The references are relied upon as explained below.

GB 2 214 518 discloses a method of determining sperm concentration and % viability in the same sample in the same determinative routine. See Example 1, where a sample is stained with PI and the fluorescence measured (F1), the sample is then permeabilized and the intensity (F2) is measured. A subsample is measured (F5) and the % viability is calculated. F2 is also proportional to the cell count and F2–F3 is correlated with cell concentration which is measured in the course of the process, see example. The determinations are considered to be made on the same sample or subsample and the determinations are considered to be performed “substantially simultaneously” or in the same determinative routine, as the routine is a FAC scan. Buffer is used to dilute the sperm, stabilization of pH sustains viability. The purpose in this method is the qualification of sperm for use in artificial insemination, where the biological utility of the sperm could be predicted in practice. (p.1, l. 7–14).

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action: (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

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Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11, 13-29, 31-33, 36-39, 41, 43 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,559,309 [B] or JP 8-332098 [L] or Live/Dead Sperm Viability Kit [U1] or Garner *et al.* [V1] or GB 2 214 518 [J] in combination with EP 586 183 [I] or WO 93/16385 [H].

The claims have been discussed above.

The references are relied upon as explained below.

US 4,559,309 teaches the determination of the proportion of live sperm to dead or dying sperm in a sample by staining with rhodamine 123/ethidium bromide and using flow cytometry to determine viability (col. 2, l. 66). The method may be used on fresh or frozen samples (col. 2, l. 16). The method allows the differential determination of dying cells as well as live and dead cells (col. 4, l. 5-21). The diluent contains FCS.

JP 8-332098 disclose a method of determining the live/dead proportion of a sperm sample by staining with two distinct fluorescent dyes and using flow cytometry.

Live/Dead Sperm Viability Kit discloses a method of determining the proportion of live sperm cells in a sample by staining with SYBR 14 and propidium iodide and analyzed by flow cytometry. The diluent contain BSA.

Garner *et al.* teach a method of viability determination of sperm using SYBR-14 and PI.

WO 93/16385 discloses a method of determining the total number of cells per unit volume of cell sample in a flow cytometer. A known number of particles having a known light scatter signal are added to a known volume of

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sample prior to analysis (abstract).

EP 586 183 discloses a method of determining absolute cell counts in a sample using a known number of fluorescent particles added to a known volume of sample, and using a flow cytometer (Summary of the Invention).

The addition of the method of WO 93/16385 or EP 586 183 to the method of US 4,559,309 or JP 8-332098 or Live/Dead Sperm Viability Kit or Garner *et al.* or GB 2 214 518 would have been obvious because both '385 or '183 suggest and generically teach the addition of microparticles of known quantity to a known volume of cells in order to be able to calculate the absolute number of cells in a sample analyzed by flow cytometry.

With regard to the use of a 25-75nM concentration of fluorochrome stain, Live/Dead Sperm Viability Kit states in the staining protocol that the examples are provided to guide researchers in the development of their own staining protocol, and that concentrations of reagents required for optimal staining may vary depending on density and other materials in the sperm sample. 100nM SYBR 14, used in the example, is the highest concentration recommended. In the absence of evidence to the contrary, given the guidance in the prior art, one of skill in the art may optimize the concentration required.

With regard to the number of control particles used per number of cells in the sample, EP 0 586 183 suggests using particles in a range of 0 to near the concentration of cells in the sample (page 5, l. 35). This is considered to be an optimization step which is well within the purview of one of skill in the art in the absence of evidence of unexpected results.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,559,309 [B] or JP 8-332098 [L] or Live/Dead Sperm Viability Kit [U] or Garner *et al.* [V] or GB 2 214 518 [J] in combination with EP 586 183 [I] or WO 93/16385 [H] as applied to claims 1-11, 13-29, 31-33, 36, 37-39, 41, 43 and 44 above, and further in view of Clay *et al.* [W1].

The claim is further directed to the addition of PVA to the dilution medium.

Clay *et al.* teach that decrease in sperm motility due to dilution may be reduced by the addition of PVA or BSA, abstract.

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The addition of PVA or the substitution of PVA for BSA in the dilution medium in the methods of US 4,559,309 or JP 8-332098 or Live/Dead Sperm Viability Kit or Garner *et al.* or GB 2 214 518 would have been obvious when taken with Clay *et al.* who teach the advantages of such an addition.

Claims 32-34, 39, 41, 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,559,309 [B] or JP 8-332098 [L] or Live/Dead Sperm Viability Kit [U1] or Garner *et al.* [V1] or GB 2 214 518 [J] in combination with EP 586 183 [I] or WO 93/16385 [H] as applied to claims 1-11, 13-29, 31, 36-38, 43 and 44 above, and further in view of Sexton [X1] or Januskauskas *et al.* [U2] or Belorkar *et al.* [V2] or Bostofte *et al.* [W2]

The claims are further directed to the use of the determination of the concentration and proportion of viable sperm in the sample to predict fertility and as a basis to adjust AI dosage.

Sexton teach that concentration and viability of sperm in an insemination dosage are directly correlated to fertility for turkey semen. Sexton also teach the use of determination of the concentration of viable sperm to adjust the insemination dosage in order to obtain high fertility rates.

Januskauskas *et al.* teach that membrane integrity (viability) and concentration of sperm from a cryopreserved sample is directly correlated with fertility in bulls.

Belorkar *et al.* teach that sperm concentration and viable sperm % are directly correlated with fertility in bulls in fresh ejaculates.

Bostofte *et al.* teach that semen quality is a function of sperm count (concentration) and viability and that semen quality is directly correlated with fertility in humans.

The prediction of fertility based on a determination of sperm concentration and viability which is determined by prior art methods as demonstrated above would have been obvious because many in the art have shown a direct correlation between sperm concentration and sperm viability with fertility.

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Claims 35 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,559,309 [B] or JP 8-332098 [L] or Live/Dead Sperm Viability Kit [U1] or Garner [V1] or GB 2 214 518 [J] in combination with EP 586 183 [I] or WO 93/16385 [H] as applied to claims 1-11, 13-29, 31-33, 36, 37-39, 41, 43 and 44 above, and further in view of Juonala *et al.* [X2] and/or Viudes-De-Castro *et al.*[U3].

Juonala *et al.* disclose that sperm viability is directly correlated with fertility which is measured by non-return rates and litter size.

Viudes-De-Castro *et al.* disclose that sperm concentration has a direct correlation with fertility and litter size up to a threshold value.

The prediction of litter size which is correlated with fertility and predicted in the prior art by determination of sperm viability and sperm concentration would have been obvious because Juonala *et al.* have shown a direct correlation between sperm viability with fertility, of which litter size is an element and Viudes-De-Castro *et al.* have demonstrated a direct correlation of litter size with sperm concentration up to a threshold value.

One of ordinary skill in the art would have been motivated at the time of invention to make this addition of microparticles to the sperm sample in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

In short, the staining method, counting method with an addition of an internal standard and use to which the results, namely sperm concentration and viability, are employed are all known in the art and the combination of these methods is not unobvious especially because it is known that fertility is correlated with absolute sperm count as well as with viability of the sperm. Attention to the exemplified method and presentation of unexpected results might advance prosecution.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651. The supervisor for 1651 is M. Wityshyn, (703) 308-4743. The normal work

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schedule for Examiner Saucier is 8:30AM to 5:00PM Monday and Tuesday and 8:30 AM to noon on Wednesday.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. Status inquiries must be directed to the Customer Service Desk at (703) 308-0197 or (703)-308-0198. The number of the Fax Center for the faxing of official papers is (703) 872-9306 or for after finals (703) 872-9307.

A handwritten signature in black ink, appearing to read 'Sandra Saucier', with a stylized flourish at the end.

Sandra Saucier
Primary Examiner
Art Unit 1651
January 6, 2003